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ARCHIVES OF PEDIATRICS

A MONTHLY DEVOTED TO THE

DISEASES OF INFANTS AND CHILDREN

JOHN FITCH LANDON, M.D., Editor

LEADING ARTICLES IN THIS NUMBER

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CLINICAL REVIEWS

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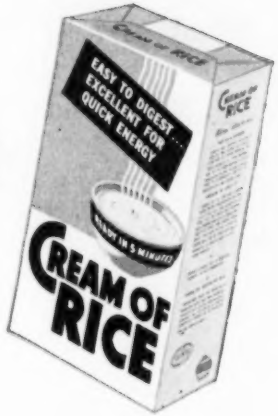

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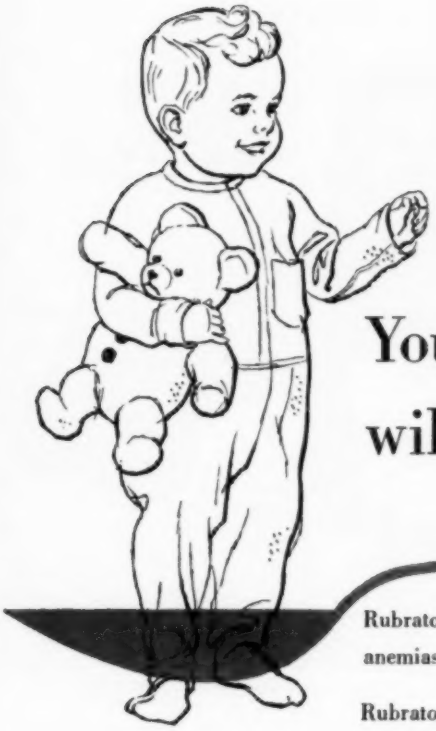

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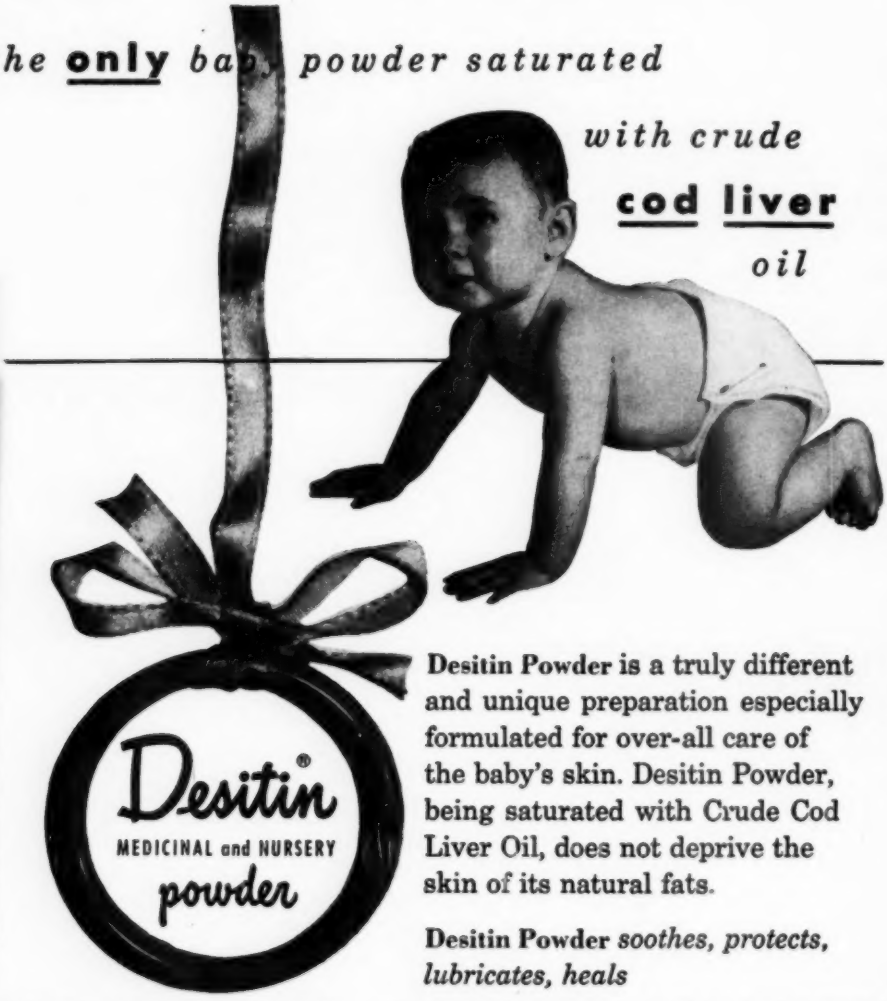

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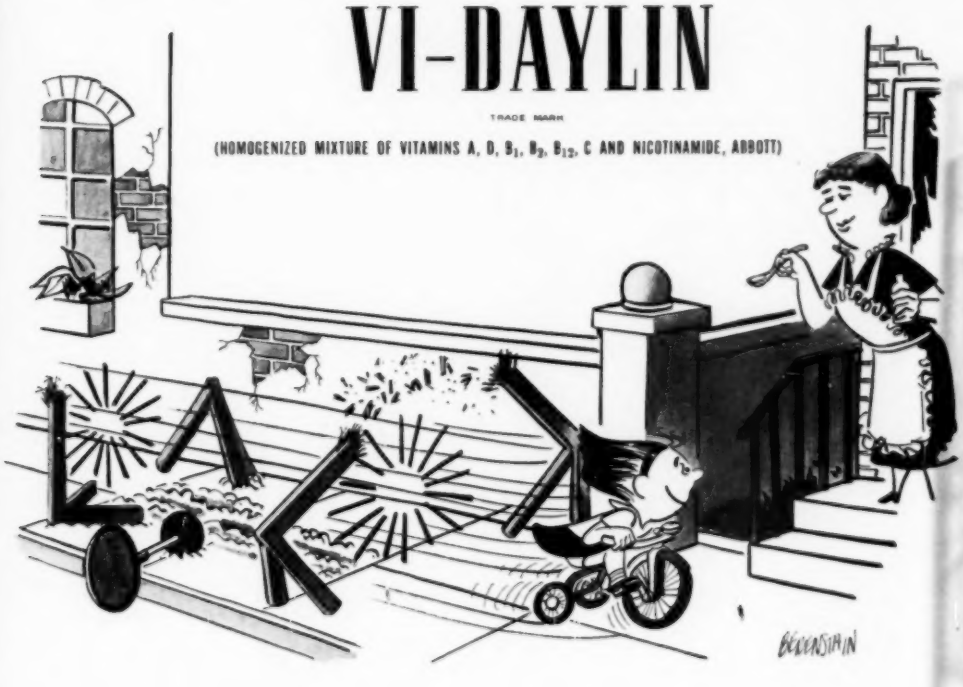

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NORM

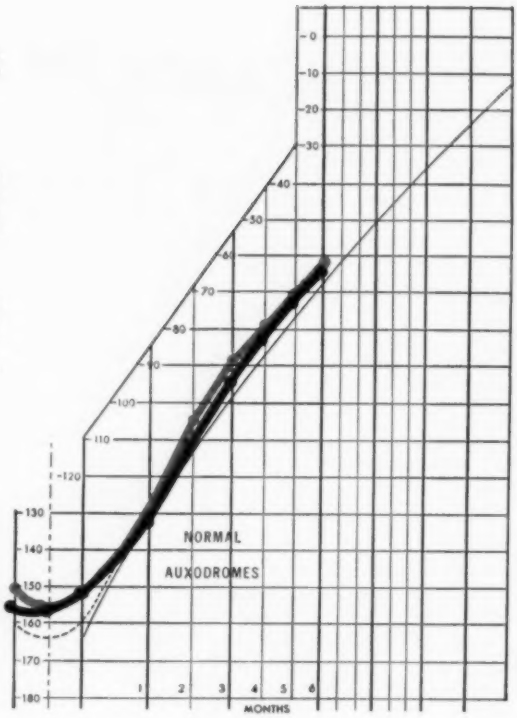
Normal schedule of development (auxodrome) plotted on Wetzel Grid.[1]

CURVE A

Composite Wetzel Grid auxodrome of 60 unselected infants on S-M-A from birth to 6 months of age.

CURVE B

Growth data, recomputed on Wetzel Grid, based on "selected subjects, most of whom were favored by environment;"[2] age: from birth to 6 months.



1. Wetzel, N. C.: J. Pediat. 29:439, 1946.
2. Jackson, R. L., and Kelly, H. G.: J. Pediat. 27:215, 1945.

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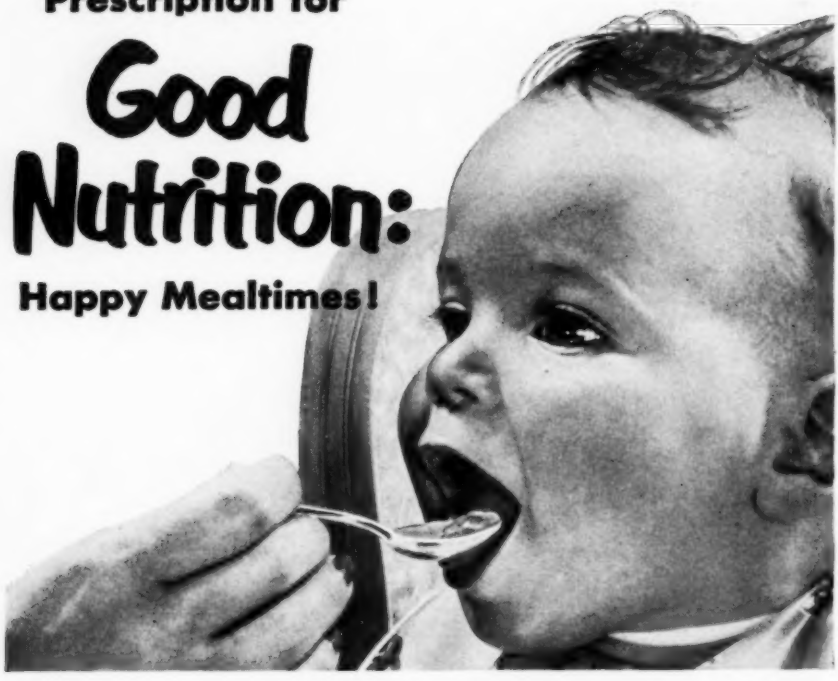

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ARCHIVES OF PEDIATRICS

VOL. 68 MARCH 1951 No. 3

JOHN FITCH LANDON, M.D., Editor

MODERN CONCEPTS OF IMMUNIZATION*

ARCHIBALD L. HOYNE, M.D.

Chicago.

It is not my purpose to discuss the theories of immunity. From a purely practical standpoint we know that some individuals are susceptible to certain infections and others are not. Moreover, we recognize that there are wide ranges of susceptibility in different individuals and also in the same individuals under varying conditions. The foregoing facts have a distinct bearing on the decisions to be made in respect to adopting measures for protection against specific diseases and the age most appropriate for instituting such procedures.

Suppose we consider first the unborn child. What prenatal infections may be transferred by the mother or what injurious effects may the mother's illness exert on the unborn? This latter subject has received unusual attention in recent years. It will be referred to again.

During the period of gestation, syphilis is the principal disease which can be conveyed by the infected mother to the fetus. Smallpox also may be acquired by the unborn child. Under the latter circumstances what happens will depend on the stage of the pregnancy. If the mother is stricken within the first few months, it is almost certain there will be an abortion. Should the infection occur during the latter months there may be a miscarriage, the child may survive an attack of smallpox in utero, it may be born

*Presented during Postgraduate Course in Pediatrics, The University of Oklahoma, School of Medicine, Oklahoma City, December 4, 1950.

with the eruption or develop the disease after birth. However, I have seen one instance where a normal baby was delivered at term on the eighth day of the mother's eruption and he did not develop smallpox. In cases of typhoid fever during pregnancy the typhoid bacillus has been known to attack the fetus and abortion follows. It has been stated, also, that the malaria parasite passes the placental barrier. That assertion has been questioned, although apparently authentic instances have been reported. In reality there are very few of the infectious diseases which the pregnant woman transmits to the prenatal child. Nevertheless at various times, some—the French in particular—have included in such a classification measles, scarlet fever and poliomyelitis. But we have had patients suffering from each of these diseases and a number of others deliver normal babies in the Cook County Contagious Disease Hospital. Infants who have one or both parents suffering from tuberculosis or leprosy are not likely to be infected if removed from the family immediately after delivery. Under any circumstances our only means for affording protection to the child before birth must consist in treating the mother which can be so successfully accomplished in the case of lues.

During the course of delivery the possibility of encountering gonococci is about the only form of infection likely to be considered and there are adequate means for prevention. But rarely, especially in forceps cases, a slight abrasion may lead to a streptococcic or straphylococcic infection and erysipelas or septicemia may follow. Also B. coli may account for a meningitis which is usually fatal.

At this point perhaps some reference should be made to German measles. Since the early Australian reports concerning abnormalities occurring in the offspring of women who experienced an attack of this disease during pregnancy—especially in the first trimester—great importance has become attached to this infection. Some obstetricians become exceedingly alarmed at the slightest rash observed on a pregnant woman. Moreover, a heavy responsibility may be placed upon the one who is called to decide whether or not a pregnant woman has German measles. This is because the decision may or may not mean the performance of a therapeutic abortion. Some physicians believe that such an operation is unquestionably indicated in the presence of German measles. On the other hand, an acquaintance who has a large obstetric practice

recently told me that he had seen a number of women who had German measles early in pregnancy and there were no instances of abnormalities when the babies were delivered. Nevertheless, on the basis of accumulated evidence, it scarcely seems justifiable to totally ignore the fact that many mothers who had German measles in the early months of pregnancy have given birth to babies who had deformities. The suggested remedy of course is to have all girls exposed to German measles before the age of puberty. Inasmuch as this disease is ordinarily of such a trivial nature there could be little objection to such a plan.

Thus far there have been mentioned some of the infections that may occur prior to birth. Under such circumstances it is obvious that the customary measures for the institution of immunity, either active or passive, are not applicable. Therefore any possible means for protecting the child must be provided directly by the mother. With this thought in mind we know that a pregnant woman who is immune to certain diseases will in some instances transmit a passive immunity to the child. Measles is an outstanding example. In most cases an attack of measles confers lifetime protection. Therefore, even if the mother had this disease in early childhood, she is still capable of passing on immune bodies to her unborn child. As a result the infant has a passive immunity which endures for at least five or six weeks as a rule. As a matter of fact, measles is rare under three months and uncommon before six months. On account of the reasons cited and because most people have had measles before reaching adult life, there is generally slight cause to fear the possibility of this disease in early infancy.

Now let us enumerate some of the common infectious diseases that may be acquired during the first few weeks of life. Previously smallpox was alluded to and is included in this group regardless of whether the mother had ever been vaccinated. In other words, it is proper to assume that the mother conveys no immunity to her child against this virus infection. Consequently every infant at birth should be regarded as susceptible to smallpox. The latter opinion also pertains to chickenpox and I have seen this disease in eight-day-old babies when the mothers had varicella at the time of delivery.

Erysipelas in the newborn used to be a fairly common occurrence but now it is seldom witnessed. Possibly this lowered incidence

may be explained partially by improved aseptic technique in the delivery room. But another streptococcic infection, scarlet fever, has also shown a sharp general decline. However, in our contagious disease hospitals, scarlet fever has always been comparatively rare under one year of age. There is no reliable method for active immunization against erysipelas at any age. Furthermore, it is a nonimmunizing disease. One attack seems to predispose to another. Meningitis of various kinds may occur at any time after birth and the same statement holds true for tetanus.

When diphtheria was prevalent the average infant was immune to this disease when it entered the world. This was because most adults possessed protective antibodies which the mother conveyed to the unborn baby. However, as the child approached one year of age, its inherited antitoxin was gradually eliminated and susceptibility to diphtheria increased. Nevertheless, rarely diphtheria of the umbilicus was encountered before the stump had healed. Moreover, only a few years ago I saw a 33-day-old infant with diphtheria of the esophagus and stomach, but very few cases of such involvement have been recorded in more than a hundred years.

Now we come to the most important of the common contagious diseases which may occur not only within the first few months but during the first few weeks of life. I refer to pertussis. It deserves special attention on account of its prevalance, high fatality rates and because the usual methods for establishing active immunity cannot be undertaken early enough to insure protection for the very young. During a period of 15 years in one of our contagious disease hospitals we had 3,081 cases of whooping cough in patients less than one year of age.

Immunity resulting from an attack of whooping cough does not persist for a long period of time as in the case of measles. Therefore, even if the pregnant woman has experienced an attack of pertussis during childhood, there is slim chance that she is capable of transmitting sufficient antibodies to afford protection to her child at birth. In order to establish an active immunity by means of pertussis vaccine a period of at least three to four months is required after the injections. Therefore it is self evident that infants during the first three to four months who most need protection are denied the benefits which may be derived from active immunization. But it seems to me there is an alternative which is

justifiable under proper conditions. This would be of course the immunization of the mother. I do not mean to imply that this idea originated with me but I have found that some highly qualified physicians are not enthusiastic in regard to such a proposal. We know from experience with human hyperimmune serum that a high concentration of antibodies can be built up by means of pertussis vaccine injections. There is also reason for believing that such antibodies would be transferred to some degree by the pregnant mother to her child. Consequently, if whooping cough is prevalent in a community and there are children in the household, immunization of the mother may be feasible if she is in a good state of health.

Reference has been made to the principal acute infectious diseases to which the newborn is ordinarily susceptible. But there are others which are witnessed infrequently. Among the latter are different forms of meningitis and very rarely poliomyelitis which has been reported earlier than two weeks after birth. All reference to epidemic diarrhea and impetigo has been omitted intentionally because they are not considered to be in the realm of our main topic.

The first protective measure for the infant following delivery is of course instillation of silver nitrate in the eyes. But very soon the program for active immunization should begin. In view of what has been said previously antipertussis vaccine should receive primary thought. We must decide (1) whether there are any contraindications to immunization procedures; (2) at what age to begin; (3) the route employed for inoculations and (4) the period of time between injections.

First, if the child is not in good health immunization had best be postponed. If either parent is mentally deficient it may be wise to defer indefinitely whooping cough immunization. A history of some mental abnormality has been disclosed in a member of the family in many of the instances of encephalitis that have been reported following pertussis immunization. Furthermore, in any instances when a severe reaction occurs after the first injection of pertussis vaccine, it is best to abandon the idea of giving any additional doses. In two cases that I know of the physician disregarded the warning of danger and continued the injections. Both babies developed encephalitis and one died.

For a number of years the opinion was more or less common

that immunization against whooping cough should not be undertaken until after the first half year of life. The reason given was that prior to six months there was insufficient antigenic response to establish a reliable immunity. The acceptance of such a view deprived the child of protection at one of the most needed times. However, the tendency now is to begin pertussis immunization at two to three months and it has been shown that successful results can be accomplished.

Various routes have been suggested for administering antigens. The ones most commonly discussed in the order of their increased importance are the oral, intracutaneous, subcutaneous and intramuscular. The last two are the chief ones to be given preference. Those who do not give the intramuscular route first choice sometimes state when selecting the subcutaneous that the injection should be "deep subcutaneous." It has always seemed to me that intramuscular injections are less painful, local reactions fewer, less likelihood of seepage from the needle puncture and better absorption of the substance. Moreover, when using alum precipitated toxoids, the likelihood of alum cysts forming seems to be less with intramuscular injections than when the subcutaneous route is adopted.

The general tendency for some time has been to increase the duration of intervals between injections of antigens. For whooping cough, as for some of the other diseases, the doses of vaccine are usually given four to six weeks apart.

I have mentioned that some years ago it was commonly assumed that the average child at birth was immune to diphtheria. On that account it was generally recommended that protective measures be instituted at about nine months. However, as the years passed the tendency increased toward beginning inoculation nearer the close of the first six months. This action was probably influenced somewhat by the period usually chosen for pertussis immunization. And then it was found that if tetanus and diphtheria toxoids were given in combination the antigenic response was greater to each than to either one when injected singly. Soon pertussis vaccine was added to the two toxoids and the volume of each dose was reduced. As a consequence we now have the triple antigens in common usage. Moreover, it has been shown, contrary to earlier opinion, that there is good antigenic response, in a large majority of infants during

the first half year. Therefore, in a program for active immunization, the administration of the triple antigens, starting at three months, is considered acceptable. In this connection it may be mentioned that a committee on immunization of the American Academy of Pediatrics for Illinois recommended whooping cough immunization at three months, some years ago. Moreover, the report was published and circulated in 1940 by the Illinois State Department of Health.

The number of organisms in each cc. of pertussis vaccine varies somewhat according to the preparation selected. Usually there are from 15 billion to 20 billion in each cc. and the total ranges between 90 billion and 60 billion. Generally, a sound immunity is not established until three to four months after the last injection. A reinforcing or booster dose of pertussis vaccine is advisable two years later.

In the case of diphtheria, active immunization is likely to endure much longer than for pertussis. Some years ago it was reported that approximately 85 per cent. had negative Schick tests five years after being actively immunized. Nevertheless, if immunization is performed during early infancy it is well to give a booster dose of toxoid at two years and again prior to the child's entering kindergarten or school. This procedure should be done routinely rather than resorting to a Schick test.

After tetanus immunity has been accomplished the defensive mechanism of the body responds very readily to a small stimulating dose of toxoid. Consequently if an individual, who has once been immunized, suffers an injury that may lead to tetanus it is merely necessary to administer a booster dose of tetanus toxoid. In other words, tetanus antitoxin should not be required under such circumstances. In this connection it has been estimated that a booster dose of tetanus toxoid—fluid toxoid is perhaps preferable to alum precipitated toxoid under these conditions—will result by the end of a week in the body having about seven times as much antitoxin as would have occurred if 1,500 units of tetanus antitoxin had been injected. However, with children in particular, it is not always known when some minor injury occurs. Therefore to have the child fortified against the possibility of tetanus at all times some pediatricians believe that a small stimulating dose should be given annually during the early years of life.

Outside of contagious disease hospitals procedures for active immunization against scarlet fever receive very little attention nowadays.

Smallpox vaccination is one of the most important of all prophylactic procedures. At present it is very likely to be neglected because the incidence of smallpox is at such a low point in this country. Every child in good health should be vaccinated during the first year of life. In the presence of eczema or any skin disease, vaccination should be postponed unless there has been a known exposure to smallpox.

Ordinarily from three to six months is a favorable time for smallpox vaccination. Secondary infections are less likely to occur if the operation is performed during the cooler months rather than in the summer.

It should be assumed that natural immunity to smallpox does not exist. Everyone should have a primary vaccination which means a characteristic "take" that leaves a typical pitted scar. The operation should be performed by the multiple pressure method. Revaccination is advisable every five years and at any time after known exposure. The duration of protection by a single vaccination can not be told definitely because it varies in different individuals. When revaccinating if the lymph is potent there may be either an accelerated reaction denoting an insufficient degree of immunity or a characteristic take. The so-called reaction of itamunity which was accepted as a reliable indication of vaccinal status for many years is regarded now as merely an allergic phenomenon.

There is no dependable method for active immunization against either measles or German measles. The use of gamma globulin for prevention of the former is often successful when administered within three days of exposure. If given later it may modify an attack of measles. Any protection afforded by gamma globulin is temporary and not likely to last for more than four to five weeks. Gamma globulin is used sometimes in a similar manner when German measles is concerned, but there is insufficient proof to show that it is of value in such cases.

Very recently a vaccine for the prevention of mumps has been introduced. I have had no experience with it. In the case of adults it may prove to be useful. For young children it would not seem

to be indicated because serious complications are very rare before puberty.

It is advisable to have the personnel of hospitals and the food handlers in hotels and restaurants immunized against typhoid and paratyphoid fevers. However, for these groups stool examinations to detect carriers are more important. Occupation is a factor that cannot be neglected. The traveling salesman is an outstanding example. Also vacationists who may journey into foreign lands or areas where typhoid exists. However, in our larger cities typhoid fever is generally an uncommon disease and routine vaccinal protection seldom seems necessary.

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INFLUENCE OF MATERNAL MEASLES (MORBILLI) ON UNBORN CHILD. (Medical Journal of Australia, Sydney, 1:835,June 24, 1950). Packer says that reports about the concurrence of rubella (German measles) in pregnant women and of congenital abnormalities in their offspring led to the suggestion that perhaps other maternal virus diseases occurring in the early part of pregnancy may also be the cause of congenital abnormalities. In 11,000 cases of measles in a recent epidemic in South Australia there were 128 married women of childbearing age; these were investigated by questionnaire. Eighteen cases of maternal measles complicating pregnancy were discovered. Twelve of the offspring were apparently unaffected. Two were born with congenital abnormalities. In both cases the maternal infection occurred during the organogenetic period. The other four pregnancies terminated prematurely. In three cases the measles was the presumed cause; in the other case the attack of measles was complicated by severe pneumonia, which was the probable cause of the abortion. The author feels that although it is unwise to attempt to generalize from a comparatively small number of cases, it seems justifiable to regard measles as in no way comparable in importance to rubella as a teratogenic agent in humans. The association of seven cases of congenital defects with measles infection during the first trimester may be merely fortuitous, and many more cases will have to be investigated before coincidence can be excluded.—*Journal A.M.A.*

INFECTIOUS ORIGIN OF ACUTE LEUKEMIA

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Several theories pertaining to the origin of leukemias have been advanced. One is that leukemias are caused by infection, another that they are neoplastic growths (the prevailing theory), and a third, that they are brought about by disordered hormonal control or metabolic imbalance.[1] A fourth theory combines the first and second, namely, that the stimulation of chronic infection may produce the neoplasm, leukemia. Rarely, other chronic irritants, like benzene[2, 3] and repeated exposure to radiation, such as roentgen rays and gamma rays of radium[2] may initiate leukemia.

This paper presents evidence for the infectious origin of acute leukemia under the following headings: 1. Preceding infection. 2. Clinical evidence of infection at onset. 3. Age incidence. 4. Early response to antibiotics. 5. Seasonal variations in incidence. 6. Geographical distribution.

1. *Preceding Infection.* Some type of infection precedes acute leukemia in a high percentage of cases.[4-11] It would seem that the more closely the early course of leukemias is observed, the more certain infection is found to precede. In all 14 carefully reported cases of Sacks and his associates[11] there was an antecedent infection or pain in the extremities. Warren[9] and Mills[12] find antecedent infection in more than 50 per cent; Pierce[10] in 49 per cent. Pierce states that these patients failed to recover normally from the antecedent infection, concluding there is "presumptive evidence that some relationship exists between infection and leukemia."

The infection preceding leukemia is usually of the upper respiratory type[10, 12], and includes "colds that hang on"[9], pharyngitis and tonsillitis,[11, 13] sinusitis[4, 13a] and otitis media.[11] Other types of antecedent infection reported are pneumonia[11] and scarlet fever.

In those cases where a preceding infection is recognized, the early course may be aleukemic[10, 14]. This finding suggests that toxins may first suppress the formation of leukocytes, not unlike a similar suppression of thrombocytes in purpura after an infection.[15] Indeed, the platelet count in acute leukemia is almost invariably decreased[14, 16], implying a toxic effect on the megakaryocytes[17, 18]. Haden[19] points out that in acute cases of leukemia the

bone marrow may be aplastic and "can be explained only on the basis of a toxic effect on the bone marrow."

2. *Clinical Evidence of Infection at Onset.* The theory of the infectious origin of leukemia gains chief support from clinicians who have noted the similarity of the clinical and pathologic picture of leukemia to that of an infectious process (Turk; Herz; Naegeli; Cabot; Sternberg; Baar and Stransky).

At the onset of leukemia one frequently finds such evidence of infection as rheumatic swelling of joints and even arthritis, cervical adenitis, fever, increased sedimentation rate, increased basal metabolic rate, albuminuria and casts, and increased capillary fragility. Rarely, blood cultures may be positive for alpha[19] or beta[13] hemolytic streptococci. Some of the above signs of infection are discussed briefly.

Rheumatic phenomena. Rheumatic pains[11-13, 19-26] are frequently the earliest manifestation of leukemia, causing confusion in diagnosis. They occur in joints[27] and muscles and may be generalized and migratory[23, 25], occasionally progressing to arthritis[19]. Landolt[28] reported rheumatic pains in 10 of 48 cases of leukemia in children, and Sacks[11] in 6 of 14 cases.

Cervical adenitis is almost always present immediately before or at the onset of leukemia[4, 11, 12, 22, 29]. Of Sacks' 14 cases, cervical adenitis was specifically mentioned in 10, and general lymphadenopathy (presumably including the cervical nodes) was noted in 3 others. Love[4] noted enlarged cervical nodes in 71 of 152 cases of leukemia. Cervical adenitis was uniformly present in 4 cases under my observation.

Increased basal metabolic rate[30, 31] in leukemia suggests infection or hyperthyroidism. The rate is increased sometimes in proportion to the severity of the process. Hyperthyroid symptoms may occur, such as exophthalmos, sweating, tachycardia, loss of weight and nervousness.[32]

Urinary findings. Albumin and casts are found in about three-fourths of cases.[33]

Increased capillary fragility, even in the rare cases without thrombopenia,[24] is evidence of infection. I reported that the most common symptom in non-selected patients with marked capillary fragility is joint and muscle pain due to infection[34], and that streptococcus toxin is the usual cause of this fragility[34-36].

3. *Age Incidence* of acute leukemia shows a marked similarity to the incidence of infections at the same age. Analyzing 1,500 cases of acute leukemias in children, Cooke[37] shows a graph in which the age incidence curve of acute leukemia closely parallels the same curves for measles and diphtheria, highest incidence being noted in all three diseases at ages 2, 3, 4 and 5 years. Upper respiratory infections, such as tonsillitis, otitis media and pharyngitis, are very frequent in this age group and usually precede the onset of leukemia, as already noted.

4. *Early Response to Antibiotics.* Heinle[38] considers the use of penicillin an important part of the treatment of acute leukemia. Miller and Turner[1] observe: "Not infrequently one of the antibiotics may abolish fever," a result not to be expected except in infection.

5. *Seasonal Variations in Incidence.* The time of onset of acute leukemia can often be determined accurately. Indeed, unlike neoplastic process, Opitz[39] finds that "the exact day of the onset of the disease can often be reported."

Lawrence[3] and Engelbreth-Holm[40] note the greater incidence of the onset of leukemia in the winter and spring. Lawrence states: "In a group of 91 patients with leukemia it was noted that 63 apparently had an onset in the winter or spring." Of 14 cases of Sacks seen in 1948 and 1949, 13 had an infection between February and June, immediately prior to the onset of acute leukemia.

6. *Geographical Distribution.* Mills[41] states that leukemia "is almost exclusively a cool climate disease." Lymphatic leukemia is extremely rare in the tropics[42] but myelogenous leukemia does occur. DeLangen states that he has never seen the acute form of leukemia in Netherland India[42]. Petersen[43] presents a map showing American mortality statistics, a distinctly greater incidence being found in the northern states, and notes a similar distribution in Europe "where there is increasing mortality when we proceed northward from Italy to Sweden."

Seasonal and geographical variations, as noted above, are to be expected in diseases initiated by respiratory infection. One would not expect these variations in neoplastic diseases of non-infectious origin.

SINUSITIS AS FOCUS

Despite its ubiquity, sinusitis in children is frequently overlooked

and is thus untreated. That active sinusitis may be a common precursor to leukemia is suggested by the following evidence.

Of four cases under my observation, chronic pansinusitis was present in all. There was shifting nasal obstruction, the dependent nostril tending to close. As a result, all were mouth breathers. Sinus tenderness to palpation and to percussion was present in all.

"Colds that hang on," noted by Warren, and recurrent upper respiratory infections, such as tonsillitis and otitis media, preceding leukemia, suggest the presence of chronic sinusitis[44-48]. These symptoms were noted in my cases as in others reported in the literature. Pneumonia and scarlet fever, which occasionally precede leukemia, are complicated by sinusitis in from 91 to 100 per cent of cases, as previously reported[45] after a review of the literature[49-51].

Puffy eyelids without urinary abnormality may be seen in either leukemia or sinusitis[11, 52, 53]. Prolonged recumbency favors puffiness of the lids on the dependent side in active pansinusitis, and was present in 3 of my 4 patients with leukemia.

Rheumatic pains in leukemia are usually caused by sinusitis. Endocarditis and myocarditis are common findings in leukemia; together with rheumatic pains, they strongly suggest a rheumatic origin, despite reluctance on the part of clinicians to diagnose two diseases, leukemia and rheumatic carditis, in the same patient.[54] The source of the rheumatic pains in leukemia is probably streptococcus toxin located in chronic sinusitis, present in 100 per cent of our rheumatic children.[45] When the diagnosis of rheumatic fever is made, before leukemia is suspected, bed rest is advised. During recumbency these toxins accumulate in the sinuses and are then forced to the cervical glands[55]. Pus under tension is a major characteristic of a focus of infection. Streptococcal toxins in pus confined in the sinuses enter the lymphatics and finally reach the blood stream, muscle and joints.

Cervical adenitis secondary to sinusitis was present in my four cases of leukemia. Cervical adenitis was present also in 88 per cent of rheumatic children, and was secondary to sinusitis. That the tonsils and teeth were not the source of the adenitis in our rheumatic children may be inferred from the fact that 86 per cent had been tonsillectomized and all had their teeth placed in good repair[45].

Since chronic sinusitis is readily amenable to treatment, even though incurable, it may be good prophylaxis against leukemia to treat the cervical adenitis and rheumatic pains preceding leukemia,

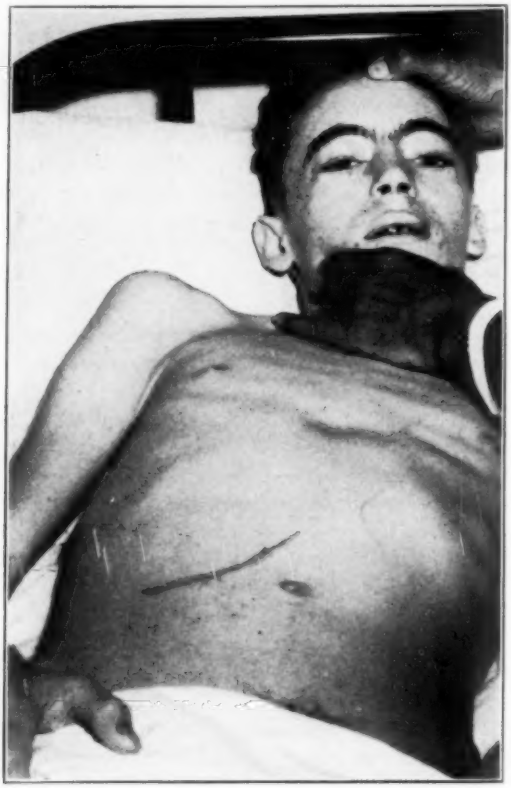

Fig. 1. Acute lymphatic leukemia following pansinusitis. Ten days before death. Note enlarged liver and spleen and mouth breathing due to nasal obstruction of sinusitis. Control pressure on forehead reveals no tenderness.

by an attack on the sinuses. Briefly, this is accomplished as follows: Drainage of purulent secretions is obtained by the head-up posture and avoidance of prolonged recumbency[55], use twice daily of proper nose drops (ephedrine sulphate 1 per cent in normal

saline solution) followed by hot wet towels to the face, first applying cold cream. Chilling, fatigue, allergens and undue excitement are to be avoided. Several streptococcic vaccines have been

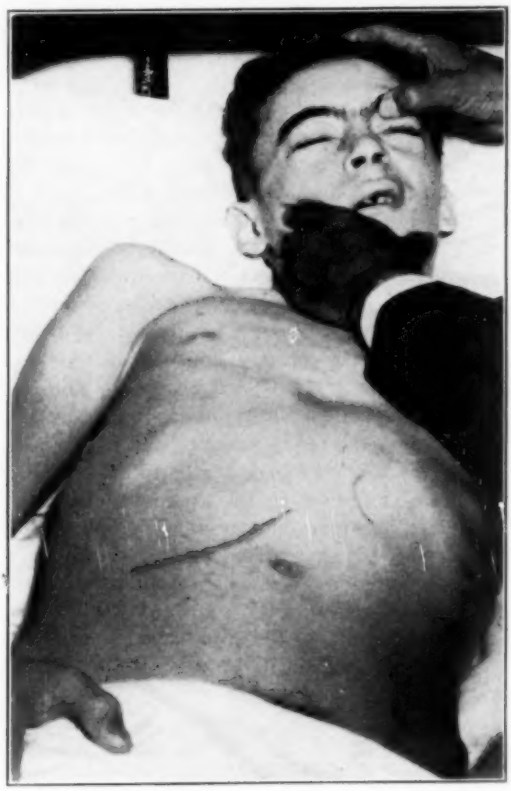

Fig. 2. Equal pressure over left frontal sinus reveals marked tenderness.

used successfully to reduce the number and severity of colds[11] despite many reports critical of this procedure.

CASE REPORT

Youth, aged 17, (Figs. 1 and 2) developed an upper respiratory infection in January 1949, from which he never recovered. He

sniffed and hacked constantly until his death of acute lymphatic leukemia six months later. In April he developed fever (103° F.), shifting pain and swelling of joints, enlarged liver and spleen, cervical adenitis and later generalized lymphadenopathy. He was treated by several physicians for rheumatic fever with bed rest, salicylates and many transfusions, but continued to become weaker and more anemic.

Laboratory findings ten days before death were: White blood cells 39,500; 98 per cent lymphocytes, 1 per cent polymorphonuclear, 1 per cent stab. Red blood cells, 1,750,000; hemoglobin 35 per cent. Sedimentation rate, 75 mm. in one hour.

Of particular interest was the possibility that the parents may have evaluated properly the cause of his illness. The mother said: "I tried to interest the doctors in his constant sniffing and clearing his throat, but they did nothing for it." The parents were convinced of the relationship between his nasal infection (sinusitis) and his illness, since the constant sniffing had never been noted before January 1949.

Conclusion. This patient illustrates eight facts commonly observed in acute leukemia: (1) his youth (most cases are under age 20); (2) his residence in a northern state; (3) preceding upper respiratory infection, in this case, acute sinusitis, which became chronic; (4) winter onset of infection and development of leukemia in spring; (5) presence of rheumatic pains and diagnosis of rheumatic fever which did not respond to medication; (6) presence of cervical adenitis secondary to pansinusitis (tonsils were absent); (7) mouth-breathing secondary to nasal obstruction of sinusitis; (8) rapid sedimentation rate probably due to infection rather than to anemia.

DISCUSSION

Wiseman's[56] view is that many acute leukemias "are simply a vigorous cellular response to infectious agents conditioned by the host, the infectious agent, or both." Infection prior to the onset of acute leukemia may be the incitant of the "vigorous cellular response." One may draw a parallel in the "leukemoid reactions" after pertussis, where temporary lymphocyte counts up to 60,000 may be seen. Pisciotta[16] notes that "certain pyogenic infections on occasion may produce white counts as high as 100,000, with even

a few myelocytes or a few blasts in the peripheral blood." The fact that most acute leukemias are recognized in the winter and spring months suggests the possibility of a predisposing and continuing irritant during the preceding cold months. Through its streptococcal toxins, sinusitis may well provide the irritant to initiate leukemia.

It is entirely possible that infection can initiate neoplasm which, once established, is irreversible. In another neoplastic disease, carcinoma, the role of preceding infection can hardly be overestimated. There is a three hundred fold difference in the incidence of cancer in ulcerative colitis as compared with the general incidence of carcinoma of the intestine.[57] Two factors emphasize the carcinogenic role of infection: (1) the youth of the patients with ulcerative colitis who develop cancer[58], and (2) the tendency of carcinomas in ulcerative colitis to be multiple[57, 59].

Unlike carcinoma which can often be eradicated in its early stages by removing or destroying all cells, acute leukemia does not permit removal of foci (lymph and bone) where leukemia cells are being formed[60]. Cure of leukemia thus seems unlikely at present. It therefore seems pertinent to prevent the onset of leukemia by a more vigorous attack on the infection which precedes it.

CONCLUSION

1. Acute leukemia is a neoplasm usually initiated by infection.

2. The infection is often described as of an upper respiratory type and may be caused by sinusitis. Four cases of acute leukemia observed by the writer were uniformly complicated by active chronic sinusitis.

3. Symptoms of chronic sinusitis present in the early stage of acute leukemia are pharyngitis, tonsillitis, otitis media, puffy eyelids, mouth breathing, rheumatic pains, cervical adenitis and sinus tenderness.

4. Since there is no cure for leukemia, nor is there any prospect of a cure in this type of malignancy, it is perhaps wiser to aim at its prophylaxis by treating more intensively the sinusitis and associated infections known to precede leukemia. The object in treating infected sinuses is to prevent the accumulation of pus and streptococcal toxin under tension, particularly during recumbency.

This toxin produces the cervical adenitis and rheumatic pains which precede leukemia and may be the incitant of the leukemic process. Treatment of chronic sinusitis is outlined in the hope that the development of leukemia may be prevented.

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CLINICAL REVIEW

In order to encourage the writing of clinical articles by recent graduates or senior medical students, the ARCHIVES *will publish monthly at least one such paper from the classes of Doctor Reuel A. Benson, New York Medical College, New York, and Doctor Philip Moen Stimson, Cornell Medical School, New York. Other interested medical schools are cordially invited to submit student papers for consideration.*

CONGENITAL CICATRIZING FIBROUS BANDS*

REPORT OF TWO CASES

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New York.

Congenital constricting fibrous bands about the hands and/or feet is a rare-occurring anomaly in the newborn. Johnson[1] reported one such case in 1941. Abbe[2] reported another in 1916 and Horwitz[3] reported six closely analagous cases in 1937. A survey of American literature for the past fifty years fails to reveal any other authentic cases. It is possible, however, that case reports may be in the *Quarterly Cumulative Index Medicus* under titles that do not lend themselves to a search for literature on this subject. It was the good fortune of this reporter to witness two such cases of constricting cicatrizing bands on the pediatrics ward of Metropolitan Hospital. To the eight aforementioned cases I would like to add these two cases and discuss some of the theories as to the etiology of this anomaly.

CASE REPORT

Case 1. V. L., 10-month-old Negro female, was admitted to the pediatrics ward of Metropolitan Hospital on October 11,1949 for plastic repair of congenital constricting bands of fingers and wrist of right hand.

Mother, para II, grava II, denied any previous diseases during or prior to delivery of this child. Normal nine month gestation and spontaneous delivery following six hour labor.

Child developed normally, sat at five months, walked at nine months, no teeth, no childhood diseases.

*Submitted as partial fulfillment of the requirements of the course in Senior Pediatrics at the New York Medical College, Flower and Fifth Avenue Hospitals, New York.

Mother reports that there is no evidence of a similar anomaly or any abnormality on maternal or paternal side of family and other sibling is perfectly normal.

Physical Examination revealed well nourished, well developed ten-month-old-Negro female in no acute distress, the only positive findings being lesions confined to the right hand.

About the dorsal and volar surface of the right hand there were six constricting bands. One of these, starting in front of the wrist distal to the prominence of the pisiform bone, curved around the hypothenar eminence and circled the radial border of the hand a little above the metacarpophalangeal joint of the index finger continuing across the dorsum of the hand obliquely over the metacarpals and terminating at the level of the articulation of the hamate and triangular bone. About the digits were the other five bands: at the level of the metacarpophalangeal joint of the thumb, slightly above the web of the index finger, at the level of the distal interphalangeal joint of the middle finger, at the level of the articulation of the proximal and middle phalange and at the terminal stump of the ring finger.

X-ray. Amputation through the base of the middle phalanx of the fourth right finger. Patient sent to the operating room for plastic type repair. At the time of this report, the bandages had not as yet been removed.

Case 2. C. J., 4-month-old white male, was admitted to the pediatrics ward of Metropolitan Hospital, date unknown, for constricting congenital cicatrizing bands of the fingers of both hands, and toes of the right foot.

Mother reports child was delivered in a normal spontaneous manner following an uncomplicated nine month's gestation. No significant data was obtained upon interrogating the mother and no history of any type of congenital anomaly, to the knowledge of the mother, was reported on either side of the family.

Physical Examination revealed a well developed, somewhat obese white male child in no acute distress. Pertinent physical findings are referable only to extremities. There are multiple constricting fibrous bands of the fingers of both hands with associated aplasia of the distal two phalanges of the fingers of both hands. There were multiple bands about the second and third toes of the right foot. Patient also demonstrated a left hydrocele.

Diagnosis. Congenital constricting bands of fingers and toes, syndactly, aplasia, auto-amputation of distal two phalanges of the fingers, and left hydrocele.

CLINICAL DESCRIPTION AND CORRECTIVE SURGERY

Annular grooves and congenital amputation:[1, 8] This condition is not similar to amputation as a result of intra-uterine bands; these annular grooves are merely ring-shaped defects. These ring-like grooves may be shallow in the skin and subcutaneous tissues only, or they may involve the deep fascia and periosteum. They are single or multiple, and occur often in the central or lower part of the forearm and high in the upper arm. They may occur in a finger or there may be a rudiment of a finger separated from the hand by a ring. If a ring is shallow, it causes edema of the part distal to it, but if deep, it may so constrict the limb during embryonic growth that actual amputation in utero results. At birth, the only remnants of the digit may be granulation tissue or a scar, terminating the stump. Treatment is for cosmetic reasons and to relieve the edema that results from interruption of lymphatic flow. Merely excising the tissues of the groove and suturing the skin borders together fails because the scar contracts, reproducing the constriction. Instead, after excising the tissues of the groove, we should aim to create as broad and as long an approximation of subcutaneous tissue and skin as possible by making diagonal cuts alternately in each skin margin to the deep fascia then undermining the skin and subcutaneous tissue for a distance in the plane between the deep and superficial fascia. The skin and whole thickness of subcutaneous tissue are brought together broadly and crowned so that a zigzag juncture is made. This succeeds by avoiding a circular constricting scar, and furnishes a maximal area of contact for re-establishing lymphatics. In some, it is safer to work in two stages, reconstructing half the ring at one time.

ETIOLOGY

Defects similar to those in cases presented have been classified by other authors under the general heading "spontaneous intra-uterine amputations." Many theories have been proposed to explain the development of constricting fibrous bands which may partially sever or completely amputate a finger, toe, arm or leg.

The most important of these etiological explanations are:

1. Ainhum.
2. Relation to premature loss of amniotic fluid or to amniotic bands.
3. Amputation by umbilical cord.
4. Defective central nervous system development.
5. Disturbance of the endocrine mechanism controlling bone formation.
6. Focal necrosis of limb bud tissue.

Ainhum (to saw or cut), studied by Horwits and Turick,[1] is a disease consisting of slow gradual linear strangulation of one or more toes, especially the fourth and fifth, eventually resulting in spontaneous amputation. This condition is usually seen in Negroes, but has been reported in the white race. It differs from congenital cicatrizing bands in that it does not occur prenatally.

Duncker, Linzenmier and Brandes[4] believed the premature loss of amniotic fluid was a likely cause of congenital bands.

Berkeley et al.[5] thought that amniotic strips of bands may, by constricting and cutting off blood supply to involved extremity, cause amputation. The possibility of the umbilical cord encircling an extremity and resulting in amputation in utero is held by the laity and by many physicians, but it does not seem possible that this degree of tension would not also result in complete obstruction of fetal circulation and fetal death. Abbe[2] offers these statements to dispute the belief of intra-uterine amputation caused by the umbilical cord: "The digits of an infant could not well be amputated by a cord with a diameter several times as great as that of the digit even if it could be made to surround the digit. Again, if the cord or even an amniotic band caused the amputation of a member, it would be reasonable to expect that occasionally the amputation would be completed near enough to term to show a fresh wound or partial amputation at birth." The reports fail to make mention of these conditions in practically every instance. It is the belief of Abbe and Variot that this non-development is due to a deficiency in the control of the developing tissues of the central nervous system. Variot, in 1890, corroborated this theory by demonstrating in one case the conspicuous atrophy of anterior and posterior horns of the spinal cord on the side corresponding to the deformity in the hand.

Streeter[6] in a monograph states that the primary etiology of intra-uterine amputations is not due to constricting bands in utero, but that they are primary congenital changes due to an abnormal constitution of germ-plasm. He believes that there is no evidence that this condition is due to amniotic bands, adhesions or mechanical constriction, but that there is a normal disparity in the quality of vitality of different tissues of the body which is adherent in the germ-plasm. He also believes that a defective development of circumscribed areas of the limb bud tissues in the embryo are of such inferior quality that imperfect histio-genesis occurs. Whether injured or defective in some way, these are maintained only through the early weeks of pregnancy. By the fourteenth week they become fibrous masses sloughing away from the normal adjoining tissues. At birth, an adjustment has been made and one finds traces of damage in the form of depressions, grooves and healed stumps, occasionally with slender strands of hyalonized material still adhering to the affected regions. It is this material which has been mistaken for amniotic bands. In many cases in which annular zones are not deep enough to interrupt the circulation, the only defect is the presence of a crease. If this theory is valid, then our cases demonstrate such a condition where there was progression after birth and the constricting bands or creases interrupted the flow of blood and lymph to lead to further degeneration of the distal stump.

Bragg[7] carried this theory of germ-plasm deficiencies into the laboratory and demonstrated on the descendants of mice treated with x-ray, a high percentage of congenital defects. Included in the anomalies were club feet, polydactalyism and hypodactalyism. Although there were no demonstrable analagous lesions to those presented in this paper, the association of deficient germ-plasm and hereditary anomalies is certainly worth consideration.

SUMMARY

Two cases of spontaneous congenital amputation of the fingers with annular ainhum-like bands and constriction of the distal portion of the phalanges with edema have been described. Possible etiological factors have been discussed. The congenital anomaly is conspicuous in the literature by its absence of actual case presentation. The literature from 1916 to the present time, barring some foreign papers which were not available, reveal approximately

eight such cases. To this I would like to add the two presented in this paper.

The most plausible explanation for this condition is presented by Streeter: that focal necrosis of the limb bud tissues occurs during the developmental embryonic stage, and that the damage occurs during the first five weeks of embryonic life. The residue are apparent at birth. The absence of several fingers in my cases may have occurred in early embryonic life as a result of this focal necrosis. Further amputations were not present because the process may have stopped in time.

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MENINGEAL REACTION IN RHEUMATIC FEVER. (Revista di Clinica Pediatrica, Florence, 47: 529, Aug. 1949). Nassi directs attention to the importance of the benign types of meningitis which appear early in the course of the first attack of rheumatic fever. They disappear within three days in the majority of the cases. There is headache, stiff neck, the Kernig, Brudzinski and Lasèque signs and red dermographism. The cerebrospinal fluid suggests either serous or lymphocytic meningitis. Relapses occur and may cause blindness or death or the disease may develop into subacute or chronic meningitis. The treatment consists of spinal taps and of intrathecal administration of small doses of penicillin or streptomycin. Treatment of the first acute attack of rheumatic fever consists of administration of penicillin, sulfanilamide, sodium salicylate and vitamin C. This is continued for one month after control of the acute symptoms in order to control the rheumatic manifestations and the residual meningeal inflammation. Fourteen cases between the ages of 4 and 10 years are reported.—*Journal A.M.A.*

PEDIATRICS HALF A CENTURY AGO

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

THE SYMPTOMS OF STATUS LYMPHATICUS IN INFANTS AND YOUNG CHILDREN*

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A very extensive literature exists upon the subject of enlargement of the thymus gland and its connection with sudden death or with death without other lesions sufficient to account for such a result. Almost all of this, however, deals with the pathological findings and with arguments for and against the possibility of death being caused by the mechanical pressure of the thymus gland.

In the beginning of the last century Millard's and Kopp's thymic asthma occupied much of the attention of physicians in every country and it was endlessly discussed until Friedleben by his dictum, "Es giebt kein Asthma thymicum," put a stop to almost all mention of it for several decades. More recently the subject has been renewed with the chief emphasis upon its pathological side. This is not strange, in view of the fact that the majority of these patients die sudden deaths and hence are seen by pathologists rather than by clinicians.

The peculiar advantages afforded at the New York Foundling Hospital have given me the opportunity during the last eight years to observe more than 25 of these cases, many of them clinically as well as postmortem.

It is necessary at the outset to define what is to be considered an abnormal enlargement of the thymus gland. This point has been debated without limit. Observers have varied greatly in their estimate of its normal weight and many have used Friedleben's statistics, almost always misquoting him, for he distinctly says in regard to one of his tables that the averages were made up by weighing the glands of only healthy, well-nourished individ-

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uals who had suffered sudden death. Of course, in this way were included the enlarged glands of those cases now under discussion.

The extensive observations of Bovaird and Nicoll obtained by weighing the glands of 495 children under the age of five years have shown that the average weight of the thymus gland at autopsy is, during the first two years, about 6 grams, and that this gland does not apparently increase in size during the first two years, but at the end of that time diminishes somewhat. These findings are also almost in accord with similar observations made by Friedleben. We may consider, therefore, any gland weighing more than 10 grams distinctly pathological; but in order to err on the side of conservatism, I have only included in these observations those children with glands weighing at least 15 grams.

The autopsy appearance of this condition is well known. The thymus gland is very greatly enlarged and is at once the striking feature of the case. It extends from a short distance below the thyroid, so low in marked cases as almost to cover the heart. Usually consisting of two lateral lobes, there may be a well-developed third lobe. The weight varies from slightly above normal to 40 grams or more. No *clear* evidences of compression of trachea or bronchi have I ever seen and they have been but seldom reported. A few very small hemorrhages may appear on the surface of the gland; these are also to be seen in sections, and there may be found one or more pockets containing a few drops of gelatinous pseudo-pus, socalled thymic abscesses. All the lymphoid tissue of the body is hyperplastic, the tonsils and adenoids, the superficial as well as the deep lymph nodes. The spleen usually shows a great enlargement from one and one-half to three times its normal size, and in its cross section are seen the very greatly enlarged Malpighian bodies standing out like sago grains. Peyer's patches and the solitary follicles of the intestines also participate in the process. A microscopical examination shows nothing characteristic; the changes are merely a hyperplasia of structures normally present. The enlargement of the thymus gland is the characteristic finding; a great enlargement of this may be found without much involvement of the other lymphoid structures, but a great hyperplasia elsewhere and not in the thymus is practically never seen.

The symptoms exhibited by children suffering from this condition are many, but it seems to me that they enable us to make

a division into several different classes. The first one is characterized by sudden death with or without some trifling shock, such as the beginning of anesthesia or the giving of antitoxin. There are practically no symptoms. The child turns over and dies or is found dead in bed; sometimes there is a cry, a slight convulsion or cyanosis. This is by no means rare; in fact, it is very common. Dudgeon, with a large experience in London, referring to the many children "found dead" who come into the coroner's hands with the diagnosis of "overlying" by their mothers, says that in his experience most of these are good examples of the lymphatic diathesis. Of this class, it is not necessary for me to describe personal cases, though I have performed autopsies on several who have died practically without a struggle, when lying on a bed or in the arms of their mothers or nurses. These babies have all been fat and well nourished. At times the fatal result is delayed somewhat longer and the cyanosis and rapid respiration may be noticed for five minutes or more. Careful inquiry has failed to satisfy me, however, that these children have presented symptoms of tracheal obstruction.

The second class presents the most characteristic symptoms, and from these, at times, we are enabled to make an accurate diagnosis. These children are usually well nourished, but not always so, and frequently rachitic. With or without some slight previous indisposition, the child suddenly becomes very ill. There may be vomiting or slight diarrhea, but the digestive symptoms are always in the background. The respiratory symptoms are prominent; there is usually very rapid, gasping respiration with cyanosis which may be marked; occasionally there is an incessant cough. The dyspnea is out of all proportion to the physical signs; these consist usually of a few scattered râles, increasing in number as the heart grows weaker. The child is generally unconscious; attacks of convulsions are usually seen and often are continuous. The pulse is of fair force at first, but becomes very rapid and feeble toward the close. The temperature is, in the great majority of cases, very high, 104° F. to 107° F., or even higher. It is somewhat affected by efforts to reduce it, but soon rises again. The dyspnea is not an obstructive dyspnea. These symptoms last from a few hours to thirty-six or forty-eight hours, the usual length being about twelve hours. The breathing becomes more

rapid, the temperature rises constantly, sometimes to 100° F.; the pulse becomes more feeble and eventually the child dies, the convulsions often persisting to the end. Such a case would pass as a good example of acute congestive bronchopneumonia, and as such, I believe, they are usually considered. The striking points are the dyspnea and cyanosis without sufficient pulmonary involvement to explain them, the convulsions and the very high temperature.

A history will illustrate this better than I can describe it:

F. U., a well-nourished child, four months old, was returned to the Asylum one afternoon with a slight coryza. His temperature was normal. At four o'clock the following morning he suddenly developed dyspnea with rapid respirations, 80 or more to the minute, his pulse was feeble and very rapid and he was much prostrated. His temperature was 104° F. and rose in a few hours to 106° F. There were a few subcrepitant râles at the bases of his chest behind. He responded fairly well for a short time to stimulation and his temperature was reduced by cold packs but rapidly rose again, the cyanosis deepened, twitching, and finally convulsions came on and he died twenty-three hours after the beginning of symptoms. The autopsy showed a thymus gland weighing 23 grams, an increase in the other lymphoid structures and nothing else abnormal.

More difficult of diagnosis are those cases that run a prolonged course with a gradual onset. The symptoms, when fully developed, are, moreover, not distinctive. There are attacks of dyspnea lasting minutes or hours, alternating with periods of easy breathing. No explanation for the dyspnea can be found and cyanosis of all grades of severity may accompany it. There may be at times entire cessation of breathing for a short period with most intense cyanosis. The lungs are clear and intubation and tracheotomy, that have often been performed, have not had the slightest effect in relieving dyspnea. In the periods of quiet breathing, however, the respiration and pulse may be irregular, and this may lead to the diagnosis of tuberculous meningitis. The temperature is usually low, 100° F.-102° F., sometimes even subnormal. The children are more or less stupid and convulsions may occur at any time, but are more common at the close, death frequently taking place in the midst of one.

An example of this class is the following:

A well-nourished boy, seven months old, was admitted to the hospital for convulsions. Two nights before admission he had had eight convulsions in the course of as many hours. He was free from these for twenty-four hours and then they began again. After admission he had several short general convulsions, and between them was somewhat rigid. He vomited most of his food. Sodium bromid controlled his convulsions somewhat, but he was very restless and had much twitching. With the exception of the vomiting, which ceased after three or four days, the digestive symptoms were never marked. His stools were always good. His temperature varied between 98½° F. and 101½° F.; it was usually between 99° F. and 100° F. On January 8th, three days after admission, he had much dyspnea, was cyanosed, and his pulse became weak and irregular. His recovery from this was rapid. Two days later he had another cyanotic attack which lasted eight minutes, and still another lasting five minutes. Thereafter the attacks of cyanosis became more frequent, six or eight in the course of twenty-four hours. He seemed somewhat hyperesthetic, but lay quiet unless disturbed. He coughed somewhat and there were scattered râles in his chest, but at no time was there consolidation. The attacks of cyanosis, with occasional slight convulsions, increased in frequency until January 14th, when he had a very restless night. He cried a great deal, but eventually went to sleep and slept quietly for nine and one-half hours and then suddenly died, nine days after the beginning of symptoms.

At autopsy nothing abnormal was found except anemia of the brain and a very much enlarged thymus gland, with the other evidences of the lymphatic diathesis.

The frequency of enlarged thymus has often been remarked at autopsies on diphtheria patients. Daut, from Escherich's clinic, and others have called attention to this fact. Elser found this to obtain also with epidemic cerebrospinal meningitis. This is also true with other diseases, and in some their course is decidedly modified by the lymphatic state. There can be no doubt that this means that such children are less resistant to infection and succumb easily.

Thus: A well-nourished child, seven and one-half months old, vomited once or twice and had rather frequent green stools. Her temperature was 102° F. when she was brought to the hospital.

The fever rose to 104° F. and her condition became correspondingly worse. The following day there was only one movement, not of a bad character and no vomiting, but her temperature rose to 108° F. and the child died. At postmortem there was found a beginning ileocolitis and also a decidedly enlarged thymus.

A much rarer form in children is that associated with purpuric symptoms, hemorrhages into the skin and elsewhere. Acland and Lochte have described such cases in young adults. I saw the following in a child:

A well-nourished but anemic boy, four years old and slightly deficient mentally, was considered in perfect health until the morning of August 4th, when after being lifted out of bed he could not stand and fell to the floor. It was then noticed that he could not use his right hand or leg. His throat was red and he had a slight hemorrhage over his right tonsil. On the right cheek there was an ecchymotic spot about the size of a half dollar. There was no history of injury. Scattered over his back were several ecchymotic spots, ranging in size from a quarter to a ten-cent piece. His gums were soft, spongy and bled easily. His pupils were equal and reacted sluggishly. There were marked weakness of the right arm and inability to use his hands well. His right leg was more affected than the arm and both wrist jerk and patellar reflex were exaggerated. The case was considered one of purpura with probably a meningeal hemorrhage. He was treated for such. In the course of the next few days he bled quite freely from his gums, his stools contained blood and his urine albumin and casts. His temperature was low, never higher than 100⅘° F., but his heart's action was always poor and always rapid, as high as 140 and more. The hemorrhages ceased for a time and then began again and a hemic murmur developed. On August 18th, two weeks after the onset, he had an attack of dyspnea and began to be rather more dull mentally. The dyspnea repeated itself from time to time. He became so comatose as to refuse food and had to be fed by gavage. Finally, on the twenty-first day of his illness, he had a sudden attack of dyspnea, throughout which his heart's action was good; he rallied from this, but another attack shortly after was fatal.

His white blood cells were counted once and were 19,600. No differential count was made.

At autopsy a thymus weighing 22 grams was found with great

hypertrophy of the lymphoid tissue of the spleen, the intestines and the lymph nodes. His nervous system was absolutely normal. Microscopically, there was no change suggesting leukemia.

There remains but to mention those infrequent cases in which the thymus acts the part of a tumor obstructing respiration and causing constant dyspnea as opposed to intermittent dyspnea, which is one of the distinguishing features of the other forms. There are several cases of recovery on record after the drawing up of this gland out of the mediastinum or the removal of the whole or of part of the thymus. These patients have no symptoms beyond constant dyspnea, existing for a long time, perhaps even from birth, and the usual results of compression of the trachea.

In these different classes of cases two symptoms stand out prominently—dyspnea and convulsions. The dyspnea, however, is seldom of such a type as to suggest obstruction; it is rather such a dyspnea as one sees in pneumonia: the stridor is lacking and there is but a moderate retraction of the soft parts. The difficulty in breathing, moreover, comes and goes, disappearing and reappearing with great rapidity. It seems impossible to believe that any actual obstruction could appear and disappear so rapidly. In the cases dying in the hospital, or out of it, I have made careful inquiry to obtain anything suggesting symptoms of suffocation, but have been unable to elicit any, and in several instances these, had they been present, could not have failed to have been noted, for some of the children died in their mothers' or nurses' arms. In those cases presenting symptoms for a longer period of time the same has been true, though the dyspnea has been at times so extreme that operative measures have been taken to relieve it, but without avail. I saw the case reported by Bovaird that died from the compression of a fatty and fibrous tumor upon the trachea just above the sternum. The dyspnea in this instance was tremendous, totally different from that in any of the thymus cases I have seen and, nevertheless, the tumor was in almost the same position as that of an enlarged thymus. Moreover, in the victims of status lymphaticus the evidences of compression upon other structures, such as the veins, with the cyanosis which one would expect to be intense in the head and neck and upper extremities, are entirely lacking. The cyanosis frequently present is of a mild grade and uniform in its distribution.

It seems to me that the negative evidence furnished by our experience at the Willard Parker Hospital is of value. We have in the course of each year all varieties of obstructive dyspnea to deal with, retropharyngeal abscess, edema of the glottis, etc. The patients are sent in not on account of diphtheria, but for their urgent dyspnea, and yet I have never seen or heard of a case treated there for obstruction caused by a large thymus.

I can add nothing to the postmortem proofs against obstruction as a cause of death so thoroughly expressed by Paltauf, but am led to dwell on the clinical evidence against this position by the article of Warthin which has recently appeared. He says that: "The symptom of chief importance is the respiratory stridor resulting from tracheal compression"; that "in those cases in which the child is found dead the phenomena of thymic asthma most probably preceded death," and that "all the symptoms and all the operative and pathological evidence point to suffocation resulting from tracheal stenosis as the chief, if not the only, cause of death." With the exception of those rare cases cured or capable of cure by drawing up the thymus, I believe these statements erroneous.

The other explanations that have been advanced as to the cause of death are, up to the present time, pure hypotheses. None of them rests upon any anatomical or experimental evidence. Svehla injected aqueous extracts of normal and hypertrophied glands intravenously and claimed to have obtained striking effects on blood pressure and cardiac paralysis. His results have not been confirmed. Dr. A. N. Richards and I tested the toxicity of an enlarged thymus. The gland, which weighed 15 grams, was completely crushed after freezing with liquid air until no cells were left intact. The powder was suspended in salt solution and 6 grams of this injected into each peritoneal cavity of two kittens. There were no symptoms noticed after this.

We endeavored to produce cytotoxins for this gland as Flexner did for lymphatic glands and bone marrow. Our results were negative, as were also Moorhead's in England.

We have undertaken experiments to test the autolytic power of the organs and the toxicity of the blood, but thus far have obtained no positive results.

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THE HISTORY OF PEDIATRICS AND ITS RELATION TO OTHER SCIENCES AND ARTS*

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The most human of all the gods ever created by the fancy or the religious cravings of mortal men was Phœbus Apollo. It was he that gave its daily light to the wakening world, flattered the senses of the select with music, filled the songs of the bards and the hearts of their hearers with the rhythm and wonders of poetry, that inspired and reveled with the muses of the Parnassus, cheered the world with the artistic creations of the fertile brains and skilful hands of a Zeuxis and Phidias—he, always he, that inflicted and healed warriors' wounds and sent and cured deadly diseases.

In the imagination of a warm-hearted and unsophisticated people it took a god to embrace and bestow all that is most beneficient and sublime—physical, moral, and mental light and warmth; the sun, the arts, poetry, and the most human and humane of all sciences and arts, namely, medicine.

Ancient gods no longer direct or control our thoughts, feelings, and enjoyments, either physical or intellectual. The kinship and correlation of hypotheses and studies, experience and knowledge are in the keeping of the philosophical mind of man, who is both their creator and beneficiary. To demonstrate this rational affinity of all the sciences and arts, some far-seeing men planned this great Congress. The new departure—in the arrangement for it—should be an example to future general and special scientific gatherings. Indeed, some of its features were adopted by the organization committee of the International Medical Congress

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which was to take place at St. Louis, but was given up on account of the limited time at the disposal of the great enterprise.

Congresses are held for the purpose of comparing and guarding diversified interests. A free political life requires them for the consulting of the needs of all classes. Scientific congresses are convened to gather and collate the varied opinions, experiences and results of many men, and to create or renew in the young and old the enthusiasm of youth. Their number has increased with the modern differentiation of interests and studies. Specialization in medicine is no longer what it was in old Egypt, namely, the outgrowth of the all-pervading spirit of castes and sub-classifications, but as well the consequence as the source of modern medical progress. It is difficult, however, to say where specialization ends and over-specialization begins, or to what extent specialization in medicine is the result of mental and physical limitation, or of the spirit of deepening research; or, on the other hand, of indolence or of greed; or whether, while specialization benefits medical science and art, it lowers the mental horizon of the individual, and either cripples or enhances his usefulness in the service of mankind. For that is what medical science and art are for. José de Letamendi is perhaps correct when he says that a man who knows nothing but medicine does not even know medicine. What shall we expect, then, of one who knows only a small part of medicine and nothing beyond?

Congresses in general have been of two kinds. They are called by specialists for specialists, or they meet for the purpose of removing or relieving the dangers of limitation. This is what explains the great success of international and of national gatherings, such as the German, British, American, and others, and what has given the Congress of American Physicians and Surgeons with its triennial Washington meetings its broadening and chastening influence.

Nor are medical meetings the only attempts at linking together what has a tendency to get disconnected. Look at our literature. The rising interest in the history of medicine as exhibited in Europe and lately also among us, and individual contributions, such as Gomperz's great book on Greek thinkers; or even lesser productions, such as Eymin's Médecins et Philosophes, 1904; or the important pictorial works of Charcot, Richet and Holländer,

prove the correlation of medicine with history, philosophy and art.

Our special theme is the history of pediatrics and its relations to other specialties, sciences and arts. Now Friedrich Ludwig Meissner's Grundlage der Literatur der Pädiatrik, Leipzig, 1850, contains on 246 pages about 7,000 titles of printed monographs written before 1849 on diseases of children, or some subject connected with pedology. Of these, two were published in the fifteenth century, sixteen in the sixteenth, twenty-one in the seventeenth, seventy-five in the eighteenth. P. Bagellardus, de aegritudinibus puerorum, 1487, and Bartholomeus Metlinger, "Ein vast nützlich Regiment der jungen Kinder," Augsburg, 1473, opened the printed pediatric literature of Europe. In the sixteenth century, Sebastianus Austrius, de puerorum morbis, Basileae, 1549, and Hieronymus Mercurialis, de morbis puerorum tractatus, 1583, are facile principes; in the eighteenth, Th. Harris, de morbis infantum, Amstelodami, 1715; Loew, de morbis infantum, 1719; M. Andry, l'orthopédie ou l'art de prévenir et corriger dans les enfants les difformités du corps, 1741; Nils Rosen de Rosenstein, 1752; E. Armstrong, An Essay of Diseases most Fatal to Infants, 1768; and M. Underwood, Treatise on the Diseases of Children, 1784; also Hufeland established pediatrics as a clinical entity; while Edward Jenner, 1798, An Inquiry into the Causes and Effects of the Variolæ Vaccinæ, opened the possibilities of a radical prevention of infectious and contagious diseases, the very subject which, a century later, is engaging the best minds and a host of assiduous workers in the service of plague-stricken mankind.

In the United States pediatrics was taught in medical schools, or was expected to be taught, by the professors of obstetrics and the diseases of women and children. The reorganization of the New York Medical College in East Thirteenth Street facilitated the creation, in 1860, of a special clinic for the diseases of the young. Instead of the united gynecologic and obstetric clinics held by Bedford, Gilman, and G. T. Elliott in their respective medical colleges, there was a single clinic for the diseases of the young exclusively. When the Civil War caused the college to close its doors forever, in 1865, I transferred the clinic to the University Medical College, and in 1870 to the College of Physicians and Surgeons. Meanwhile other medical schools imitated the example

thus presented. The teachers were classed amongst the clinical professors; only in those schools which are forming part of universities and are no longer proprietary establishments, a few now occupy the honored position of full professors; in a very few the professor of pediatrics is a full member of the "faculty."

In the English colonies of America the earliest treatise on a medical, in part pediatric, subject was a broadside, 12 inches by 17. It was written by the Rev. Thomas Thacher, and bears the date January 21, 1677-8. It was printed and sold by John Foster, of Boston. The title is "A brief rule to guide the common people of New England how to order themselves and theirs in the Small-Pocks, or measles." A second edition was printed in 1702.

Before and about the same time in which American pediatrics received its first recognition at the hands of the New York Medical College, European literature furnished a new and brilliant special literature. France, which almost exclusively held up the flag of scientific medicine during the first forty years of the eighteenth century, furnished in C. Billard's Traité des maladies des enfants nouveau-nés, 1828, and in Rilliet's and Barthez's Traité clinique et pratique des maladies des enfants, 1838-43, standard works which were examples of painstaking research and fertile observation. England, which produced in 1801 I. Cheyne's Essays on the diseases of children, gave birth to Charles West's classical lectures on the diseases of infants and children in 1848, and F. Churchill's treatise in 1850.

The German language furnished a master-work in Bednar's die Krankheiten der Neugebornen und Säuglinge, 1850-53. A. Vogel and C. Gerhardt, both general clinical teachers, gave each a text book in 1860, Hoench in 1861; and Steffen, in 1865-70, published a series of classical essays.

The number of men interested in the study and teaching of pediatrics grew in proportion to the researches and wants of the profession at large. That is why three large and influential cyclopedias, the works of many authors, found a ready market, namely, C. Gerhardt's Handbuch der Kinderkrankheiten, 1877-93; John M. Keating's Cyclopedia of the Diseases of Children, Medical and Surgical, 1889-90, and I. Grancher's and I. Comby's Traité des Maladies des Enfants, in five volumes, the second edition of which is being printed this very year.

The collective and periodic literature of pediatrics began at a comparatively early time. There was a period toward the end of the eigheenth century when the influence of Albrecht von Haller seemed to start a new life for German medical literature before it lost itself again in the intellectual darkness of Schelling's natural philosophy, from which it took all the powers of French enthusiasm and research, and the epoch-making labors of Skoda, Rokitansky, and finally Virchow, to resuscitate it. About that early time of Haller, there appeared in Liegnitz, 1793, a collection of interesting treatises on some important diseases of children (Sammlung interessanter Abhandlungen über etliche wichtige Kinderkrankheiten). France followed in 1811 with a collection bearing the title: La Clinique des Hôpitaux des enfants, et revue retrospective médico-chirurgicale hygiénique; publiées sous les auspices et par les médecins et chirurgiens des hôpitaux consacrés aux maladies des infants. Next in order are five volumes of Franz Joseph von Metzler's Sammlung auserlesener Abhandlungen über Kinderkrankheiten, 1833-36; twelve fascinoles under the title Analekten über Kinderkrankheiten oder Sammlung ausgewählter Abhandlungen über die Krankheiten des Kindlichen Alters; la clinique des Hôpitaux des enfants, Redacteur en chef Vanier, Paris, 1841; and I. Behrend and A. Hildebrandt, Journal für Kinderkrankheiten, which appeared regularly from 1843 to 1872. It gave way to the Jahrbuch für Kinderheilkunde, which appeared in quick and regular succession from 1858 to the present time. Three series of Austrian journals between 1855 and 1876 consisted of a dozen volumes only. They contain among other important contributions the very valuable essays of Ritter von Rittershayn, who deserved more recognition during his life and more credit after his death, for his honesty, industry and originality, than he attained.

Special pediatric journals have multiplied since. The United States has two, France four, Germany five, Italy two, Spain one. As long as they are taken by the profession we should not speak of overproduction. I attribute their existence to the general conviction that there is no greater need than that of the distribution of knowledge of the prevention and cure of the diseases of the young. The literature of pediatrics seems to prove it. Not 7,000, as before 1850, not even 70,000 titles of books, pamphlets and magazine articles exhaust the number.

Pediatric societies have increased at the same rate. The American Medical Association and the British Medical Association founded each a section twenty-five years ago, the New York Academy of Medicine, in 1886. The American Pediatric Society was founded in 1889, the Gesellschaft für Kinderheilkunde connected with the German Gesellschaft der Aerzte und Naturforscher in 1883, the English Society for the Study of Disease in Children, in 1900. There are pediatric societies in Philadelphia, in the State of Ohio, in Paris, Kiew, St. Petersburg, and many places, all of them engaged in earnest work which is exhibited in volumes of their own or in the magazines of the profession. If we add the annual reports of hundreds of public institutions, which are so numerous, indeed, that a large volume of S. Hügel, "Beschreibung sämmtlicher Kinderheilanstalten in Europa," was required as early as 1848 to enumerate them; and an enormous number of text books of masters, and of such as are anxious to become so, and monographs, and essays, and lectures, and notes preliminary and otherwise, which fill the magazines that most of us take or see, and some of us read—we may form an idea to what extent a topic formerly neglected has taken hold of the conscience and the imagination of the medical public.

Before 1769 there was no institution specially provided for sick children. They were admitted now and then to foundling institutions and general hospitals. In that year Dr. G. Armstrong established a dispensary in London, which was carried on until he died. A similar institution was founded in Vienna by Dr. Marstalier, in 1784. Goelis took charge of it in 1794, L. Politzer developed it, and it is still in existence. Before the French Republic was strangled, it founded the first and largest child's hospital in Europe, the Hôpital des Enfants malades, in 1802. The Nicolai Hospital was established in St. Petersburg, in 1834, by Dr. Friedburg; the St. Anne's Child's Hospital, in Vienna, 1837, by Dr. Ludwig Mauthuer; and the Poor Children's Hospital, of Buda-Pesth, in 1830, by Dr. Schöpf, Merei, who afterwards founded and directed the Child's Hospital of Manchester, England.

Since that time the increasing interest in the diseases of children on the part of humanitarians and of physicians and teachers has multiplied children's hospitals. Most of them are small, but they are numerous enough both to exhibit and disseminate the sense of

responsibility to the sick and to the necessities of teaching. The United States has been the last country to participate in these endeavors. The mostly proprietary medical schools did not find pediatric teaching to their advantage, and it took the hearts and purses of the public a long time to be opened. The waves of humanitarianism, sometimes directed by a church, and the demands of science have finally overcome previous indolence. There are many general hospitals that gradually opened special children's wards. You find pediatric hospitals in some of the larger cities—New York, Boston, Philadelphia, Albany, St. Louis, and others. It has so happened, however, that real specialties have appealed more to the general sympathy than pediatrics. That is why the number of beds in orthopedic and other special hospitals are mostly favored. Practical teaching has not been extensive. Children's hospitals that should be used for that purpose, and that are directly connected with a medical school, are but few. It has taken the medical faculties, even of universities, too much time to appreciate the necessity of special and well-regulated bedside teaching. In some instances lay trustees, guided by their medical advisers, have opened their wards before faculties have consented to open their eyes. At the present time, however, there is hardly a great medical school that does not give amphitheatre or bedside instruction, either in a children's ward of a general hospital or in a special children's or babies' hospital. To a certain extent the teaching of pediatrics in a general hospital has its great advantages. It is not a specialty like that of a special sense or a tissue. For the purpose of study it had to be segregated, but it will never be torn asunder from general medicine. Vogel and Gerhardt were both general clinicians.

The comparative anatomy and physiology, hygiene, etiology, and nosology of pediatrics have been discussed before you by one of the most prominent pediatrists of our era. It will be my privilege to explain, as far as time will permit, its relation to general medicine, to embryology and teratology, obstetrics, hygiene, and private and public sanitation, to therapeutics, both pharmacal and operative, and to the specialties of otology, ophthalmology, dermatology, and the motor system, to pedagogy, to neurology and psychiatry, forensic medicine and criminology, and to social politics.

Infancy and childhood do not begin with the day of birth. From

conception to the termination of fetal life evolution is gradual. The result of the conception depends on parents and ancestors. Nowhere are the laws of heredity more perceptible than in the structure and nature of the child. Physical properties, virtues and sins, and tendencies to disease may not stop even with the third or fourth generation. Hamburger and Osler trace an angioneurosis through six generations, the first case in the series being observed by Benjamin Rush. In many instances, stillbirths, early diseases, atrophy, and undue mortality of the young depend on antenatal happenings. The condition and diet of the mother influences her offspring. The danger of a contracted pelvis, and the necessity of premature delivery may be obviated by the restriction of the diet, or even by appropriate (thyroid and other) medication of the pregnant woman. Experience and experiment tell the same story. The continued practice of preventing conception causes endometritis. Alcoholism causes chronic placentitis, premature confinement, or stillbirth. So does chronic phosphorus and lead poisoning. Fortunately, however, the usual medication resorted to during labor is rarely dangerous, for even morphine or ergot doses given to the parturient woman on proper indications affect the newly-born rarely, and chloroform anesthesia almost never.

Scanty amniotic liquor, by the prevention of free intrauterine excursions, may cause club-foot; or close contact of the surfaces of the embryo and the membranes give rise to adhesions of the placenta and the head, to filaments and bands whose pressure or traction produces grooving or amputation of limbs, cohesion of toes or fingers, umbilical, meningeal, encephalic, or spinal hernia; not in extra-uterine pregnancy only, where such occurrences are very frequent. Even the majority of harelips and fissured palates have that origin. Arrests of development and fetal inflammation are the headings under which most of the anomalies of the newly-born may be subsumed; congenital diseases of the ear and of the heart may result from either cause or from both. Obstructions of the intestines, the rare closures of the esophagus, the ureter, and the urethra, with hydronephrosis and cystic degeneration of the kidneys are probably more due to excessive cell proliferation in the minute original grooves than to inflammation.

The insufficient closures of normal embryonic fissures or grooves

explains many cases of spina bifida, many of encephalocele, most of the split lips and palates, all of porencephalus, bifid uvula and epiglottis, pharyngeal and thyroglossal fistulæ, the communications between the intestinal and urogenital tracts, and the persistency and patency of the urachus.

Heredity need not show itself in the production of a fully developed disease. It exhibits itself normally either in equality or resemblances, either total or partial, of the body, or some one or more of its external or internal organs. In this way it may affect the nervous, the muscular, the osseous, or other tissues. That is why dystrophies in different forms, obesity, achondroplasia, hyperplasia, or atrophy may be directly inherited, while in other cases the disposition to degeneration only is transmitted.

Hereditary degeneracy is often caused by social influences. The immoral conditions created by our financial system make women select not the strong and hearty and the young husband, but the rich and old, with the result of having less, and less vigorous, children. Certain professions, the vocations of soldiers and mariners, and subordinate positions of employees in general, enforce complete or approximate celibacy, with the same result. The nations that submit to the alleged necessity of keeping millions of men in standing armies, are threatned with a degenerated offspring, for not only do they keep the strongest men from timely marriages, but they increase prostitution and venereal diseases, with their dire consequences for men, women, and progeny. Wars lead to the same result in increased proportion, for tens and hundreds of thousands of the sound men are slain or crippled, or demoralized. Those who are inferior and unfit for physical exertions remain behind and procreate an inferior race. Those who believe with Lord Rosebery that an empire is of but little use without an imperial race will always, in the interests of a wholesome civilization, object to the untutored enthusiasm which denounces the "weakling," and the "craven cowardice" of those who believe in the steady evolution of peace and harmony amongst men, and, in sympathy with the physical and moral health of the present and future generation, will prefer the cleanly and washed sportsmanship of an educated youth to that of the mud-streaked and blood-stained manhunter.

A great many diseased conditions cannot be thoroughly un-

derstood unless they be studied in the evolving being. Tumors are rarely inherited, but many of them are observed in early life. Lymphoma, sarcoma, also lipoma and carcinoma, and cystic degeneration, are observed at birth, or within a short time after, and seem to favor Cohnheim's theory, according to which many owe their origin to the persistence in an abnormal location of embryonic cells. This theory does not exclude the fact that congenital tumors may remain dormant for years or decades and not destroy the young.

So much on some points connected with *embryology* and *teratology*. The connection with *obstetrical practice* is equally intimate. Three per cent of all the mature living fetuses are not born into postnatal life this very day. To reduce the mortality even to that figure, it has taken much increase of knowledge and improvement in the art of obstetrics to such an extent that it has become possible by Cesarean section not only to save the fetus of a living, but also of a dead mother, for the fetus in her may survive the dying woman.

But after all, many a baby would be better off, and the world also, if it had died during labor. There are those, and not a few, who are born asphyxiated on account of interrupted circulation, compression of the impacted head, or meningeal or encephalic hemorrhage, which destroys many that die in the first week of life. Those who are not so taken away may live as the result of protracted asphyxia only to be paralytic, idiotic, or epileptic. Many times in a long life have I urged upon the practitioner to remember that every second added to the duration of asphyxia adds to the dangers either to life or to an impaired human existence. Besides fractures, facial or bracial paralysis, cephalhematoma and hematoma of the sternocleido-mastoid muscle, gonorrheal ophthalmia, with its dangers to sight and even life, may be daily occurrences in an obstetrician's life. All such cases prove the insufficiency of knowledge without art, or of art without knowledge, and the grave responsibility of the practical obstetrician. To lose a newly-born by death causes at least dire bereavement; to cripple his future is not rarely criminal negligence.

Within a few days after birth the obstetrician or the pediatrist has the opportunity of observing all sorts of microbic infections, from tetanus to hemorrhages or gangrene, and the intense forms

of syphilis. Not an uncommon disease of the newly born and the very young is nephritis. It is the consequence, in many cases, of what appears to be a common jaundice, or of uric acid infarction, which is the natural result of the sudden change of metabolism. The diverticula of the colon, as described by Hirschsprung and Osler, and what nearly forty years ago I characterized as congenital constipation, which depends on the exaggeration of the normally excessive length of the sigmoid flexure, belong to the same class. Their dangers may be avoided when they are understood. Of the infectious diseases of the embryo and the fetus, it is principally syphilis that should be considered; amongst the acute forms variola and typhoid are relatively rare.

What I have been permitted to say is enough to prove the intimate interdependence and connection between pediatrics and the diseases of the fetus, with embryology and teratology, obstetrics, and some parts, at least, of social economics.

After birth there are anomalies and diseases which are encountered in the infant and child only. There are also, common to all ages, though mostly found in children, such diseases as exhibit a symptomatology and course peculiar to them. The first class, besides those which are seen in the newly-born, is made up mostly of developmental diseases—scrofula, rachitis, chlorosis. The actual or alleged ailments connected with dentition, most forms of stomatitis, Bednar's socalled aphthæ, the ulceration of "epithelial pearls" along the raphe, amygdalitis, pharyngitis, adenoid proliferations, latero- and retro-pharyngeal abscesses belong here. Infectious diseases, such as variola, diphtheria, scarlatina, measles, pertussis, and tuberculosis of the glands, bones, joints, and peritoneum have been most successfully studied by pediatrists or those clinicians who paid principal attention to pedology. Meissner prints the titles of more than 200 actual monographs on scarlet fever published in Europe before 1848. Pleurisy and pneumonia of the young have their own symptomatology. Empyema is more frequent and requires much more operative interference. Tracheotomy and intubation are mostly required by the young, both on account of their liability to edema of the larynx and to diphtheria, and of the narrowness of the larynx. Of invagination, 25 per cent occur under one year, 53 per cent under ten. Appendicitis, sometimes hereditary and a family disease, would long ago have

been recognized as a frequent occurrence in the young if it had not been for the difficulty, mainly encountered in the young, and sometimes impossibility of its diagnosis. That is what we have been taught by Hawkins and by Treves, and lately by McCosh. Operations on glandular abscesses, osteotomies, and other operations on the bones and joints, particularly in tuberculosis, and on malformations, such as have been mentioned, require the skillful hand of the operating physician in a great many instances. Omphalocele, exstrophy of the bladder, undescended testicle, spermatic hydrocele, multiple exostoses, imperforate rectum, atresia of the vagina, or an occasional case of stenosed pylorus, belong to that class, some requiring immediate operation, some permitting of delay. It is principally infancy that demands removals of angioma, which are almost all successful, and of hygroma, mostly unsuccessful, mainly when situated on the neck and resulting from obstruction of the thoracic duct sometimes connected with thrombosis of the jugular vein. Childhood requires correction of kyphosis and scoliosis, and operations for adenoids and hypertrophied tonsils, and furnishes the opportunities for lumbar puncture and for laparotomy in tubercular peritonitis; also suprapubic cystotomy, and mastoid operations. That gum-lancing is no operation indicated or permissible in either the young or adult, and not any more so in the former than in the latteer, is easily understood by those who acknowledge its necessity only in the presence of a morbid condition of the gums or teeth, and not when the physiological process of dentition exhibits no anomaly. It scarcely ever does. Altogether, operating specialists would work and know very much less if a large majority of the cases were not entrusted to them by the pediatrist, who recognizes the principle that those who are best fitted to perform it should be trusted with important medical work. So well is the seriousness and difficulty of operative procedures, as connected with diseases of children, recognized by experts, that 1,500 pages of Gerhardt's handbook are dedicated to external pathology and operations, and that special works besides many monographs by hundreds of authors, have been written by such masters as Guersant, Forster, Bryant, Giraldès, Holmes, St. Germain, Karewski, Lannelongue, Kirmisson, and Broca.

Ear specialists recognize the fact that *otology* is mostly a spe-

cialty of the young. The newly-born exhibit changes in the middle ear which are variously attributed to the presence of epithelial detritus, to the aspiration of foreign material, or to an edema *ex vacuo* occasioned by the separation of formerly adjacent mucous surfaces. Pus is found in the middle ear of 75 per cent of the still-born, or of dead nurslings. It contains meconium, lanugo, and vernix. Aschoff examined fifty still-born, or such as had lived less than two hours; twenty-eight of them had puss in the middle ears (55 per cent). He also examined thirty-five infants that had lived longer than two hours; twenty-four had pus (70 per cent). Evidently the latter class had been exposed to a microbic invasion. The diagnosis in the living infant is very difficult, mostly impossible, on account of the large size of the Eustachian tube, which, after having admitted the infection, allows the pus to escape into the pharynx and the rest of the alimentary canal. Many of the newly-born that die with unexplained fevers perish from the septic material, or its toxins, absorbed in the middle ear or the intestines. Nor are older children exempt. Geppert (*Jahrb. f. Kind.*, Vol. xlv., 1897) found a latent otitis media in 75 per cent of all the inmates of the children's hospitals. Both latent and known otitis is often connected with pneumonia, or with pneumonia and enteritis. In individual cases it may, however, be difficult to decide which of the two or three is the primary, which the secondary affection.

The great vascularity of the middle ear, but still more the accessibility of the funnel-like Eustachian tube in the infant, renders otitis media very frequent. Schwartze's assertion that otitis media furnishes 22 per cent of all ear cases in general or special practice is surely correct. Besides, difficult hearing is very frequent in the young, a fact of the greatest import to pedagogy. As early as 1886 Bezold found that of 1,900 school children 25 per cent had only one-third, and 11 per cent of the others only one-fifth of normal hearing. The frequent affections of the nose and pharynx in the young explain these facts and exhibit the possibilities of preservation. Finally, the immature condition of the mastoid process and of the floor of the external canal is best appreciated by the practitioner, general or special, who deals with their abscesses.

Whether deafmutism is the result of consanguineous marriage cannot be definitely asserted. It is not often hereditary, quite

often it appears to be the result of family alcoholism, it sometimes depends on arrest of development and fetal inflammation, but is more frequently an acquired condition. Not rarely children are affected after they have been able to speak. The majority of cases are caused by cerebral or cerebrospinal inflammation. According to Biedert, 55 per cent are of that class, 28 per cent are caused by infectious diseases (cerebrospinal meningitis, scarlatina, typhoid fever, diphtheria, also variola and measles), 3.3 per cent by injuries, and only 2.5 per cent are original ear affections. Thus many of the congenital cases, and most of the acquired, are preventable. More and more will our deaf-mute institutions avail themselves of this knowledge, and will learn how to teach their children not only how to read and write, but also how to hear.

Not to the same, but to a great extent, pediatrics and *ophthalmology* join hands. Infectious diseases, such as diphtheria, affect the conjunctiva and sometimes the cornea. Syphilis of the cornea, with or without chronic iritis, is known in the form of parenchymatous or diffuse keratitis. A frequent tumor in the eye of the young is glioma, and frequent symptomatic anomalies are strabismus and nystagmus—both of them the results of a great many and various external or internal causes, with sometimes difficult diagnoses.

The connection of pedology with *dermatology* is more than skin deep; some of the most interesting problems of the latter must be studied on antenatal and postnatal lines. The congenital absence of small or large parts of the surface is probably due to amniotic adhesions; seborrhea and the mild form of lichen, also the furunculosis of infant cachexia and atheroma, to the rapid development, in the second half of intrauterine life, of the sebaceous follicles; ichthyosis, to the same and to a hypertrophy of the epidermis and the papillæ of the corium, sometimes with dilatation of their blood-vessels and with sclerosis of the connective tissue. Congenital anomalies, such as lipoma, sarcoma, nevus pigmentosus, open all the questions of the embryonal origin of neoplasms; and the eruptions on the infant surface unclose to the specialist the subject of infectious diseases. We recognize in the pemphigus of the palms and soles syphilis; in herpes, gangrene, and in what I have described as chronic neurotic pemphigus, the irritable nervous system; in eczema, constitutional disturbances of the nutri-

tion; in erythema, local irritation or intestinal autoinfection; in isolated or multiple forms, ranging between hyperemia and exudation, the effect of local irritation or the acute or chronic influence of drugs. A dermatologist who knows no embryology or pedology, a pediatrist who knows no dermatology, is anything but a competent and trustworthy medical practitioner.

The diseases of the *muscles* interest the pediatrist, the surgical specialist, the orthopedist, the neurologist, to an equal extent. Many forms of myositis are of infectious origin. Amongst the special forms of muscular atrophy it is the hereditary variety which concerns the first. The spinal neuritic atrophy, the myogenous progressive dystrophy, including the so-called pseudohypertrophy, Thomson's congenital myotonia, and (atrophy) the defects of muscles—mainly of the pectoral, but also the trapezius, quadriceps, and others—no matter whether they are primary or myogenous (this probably always when there is a complication with progressive dystrophy), are of special interest to all. I need not do more than mention torticollis in order to prove that neither the special pediatrist, nor the special orthopedist, nor the general surgeon, can raise the claim of ownership.

The relations of pediatrics to *forensic medicine* are very close. Nothing is more apt to demonstrate this than the immense literature in every language on infanticide and all the questions of physiology, physics, and chemistry connected with that subject. The monographs and magazine essays of the last two centuries written on the value or the fallacy of the lung test in the dead newly-born would fill a small library. Much attention has been paid by physicians and by forensic authors to lesions and fractures of the newly-born head, and to anomalies of the female pelvis causing them. Apparent death of the newly-born and the causes of sudden death in all periods of life have been studied to such an extent as to render negative results of police investigation and of autopsy reports less numerous from year to year. Most sudden deaths receiving the attention of the authorities occur in the young. There were (Wm. Wynn Westcott in *Brit. Med. Journ.*, November 7, 1903) in England and Wales during ten years 15,009 overlain infants; in 1900, 1,774. In Liverpool, out of 960 inquests there were 143 on babies that had died of such suffocation by accident or malice aforethought; in London, in

1900, 615; in 1901, 511; in 1902, 588. In London they had annually 8,000 official inquests, one of fourteen of which was on overlain infants. The etiology of sudden deaths would be far from complete, indeed the most difficult questions could not be solved except by the facilities furnished by the observations on the young. Foreign bodies in the larynx, beans, shoe-buttons, and playthings generally, even ascarides (Bouchut), bones and pieces of meat aspirated during vomiting, acute edema of the glottis, aspiration of a long uvula, or of the retracted tongue, the rupture of a pharyngeal abscess or of a suppurating lymphoid body into the trachea, a sudden swelling of the thymus in the narrow space between the manubrium and vertebral column, which at best measures only 2.2 cm., even a coryza in the narrow nose of a small infant filled or not with adenoids—are causes of sudden death.

The *nervous system* furnishes many such cases. It is true there is no longer a diffuse interstitial encephalitis, such as Jastrowitz would have it, nor is the hypertrophy of the brain so frequent by far as Hüttenbrenner taught, but there are sudden collapses and deaths by falls on the abdomen, by sudden strangulation of large herniæ and other shocks of the splanchnic nerve. There are sudden and unexplained deaths in unnoticed attacks of convulsions, in the first paralytic stage of laryngismus stridulus, in glottic spasms from whatever cause, in the paralysis—or, according to Escherich, laryngospasm—of what since Paltauf has been denominated status lymphaticus, in cerebral anemia, no matter whether it is the result of exhaustion or, as Charles West taught us sixty years ago, from the mere change of position of a pneumonic or otherwise sick baby, when suddenly raised from its bed. Or, death may occur suddenly (a very frequent occurrence) in the heart failure of parenchymatous degeneration of the heart muscle as it occurs in and after diphtheria, influenza, and other infectious diseases, or in the acute sepsis of appendicitis and other intraperitoneal affections, whether recognized or not. For the absorbing power, even of the normal peritoneum, is enormous. Of a very acute infection ("infectio acutissima"), Wernich spoke as early as 1883.

In gastroenteritis, the terminating bronchopneumonia may destroy life quite suddenly; there is a capillary bronchitis of the very

young with no cry, no moan, and no cough, but with sudden death; there are in extreme atrophy fatal emboli into the pulmonary, sometimes renal, more often cerebral, arteries. There are the cases of uremic convulsions, sudden, with sudden death, which are often taken to be merely reflected or "providential," because the frequency of acute nephritis in the newly-born and the infant, with its fever and its uremia, in spite of the publications of Martin and Ruge, Virchow, Orth, Epstein, and my own, is not yet fully appreciated. That is so much the more deplorable as the diagnosis of nephritis at any age is readily made by the examination of the urine, which is so easy to obtain in the young. Other suddenly fatal conditions, such as the acute or chronic sepsis I mentioned before, often quite unsupected, entering through the umbilicus, the intestine, or the middle ear, are quite frequent.

(*To be concluded in April Issue*)

AUREOMYCIN IN INFANTILE DIARRHEA AND VOMITING. (British Medical Journal, London, 1: 1398, June 17, 1950). Magnusson and his collaborators point out that Bacterium coli neapolitanum has been demonstrated in a number of epidemics of infantile diarrhea and vomiting. The present report is based on observations in two epidemics in which the presence of B. coli neapolitanum was demonstrated not only in the stools but at times in the respiratory tract of the infants with diarrhea and vomiting. During the first few days after the development of gastroenteritis fluids were given liberally. The basic food was breast milk. Penicillin and sulfonamide compounds were tried in the majority of cases in both epidemics, but they had no effect on the gastrointestinal symptoms. In several cases the gastroenteritis had its onset in the course of penicillin and sulfonamide therapy. Streptomycin was given in 17 cases, but no specific therapeutic effect was seen. Eight patients in the second epidemic were treated with aureomycin after it had been found that the bacteria were sensitive to this antibiotic. The aureomycin was given by mouth, 25 mg. six times a day. B. coli neapolitanum disappeared from the stools after a few doses of aureomycin; in a few of the cases they persisted somewhat longer in the respiratory tract. Improvement in the clinical condition coincided with the bacteriologic effects.—*Journal A.M.A.*

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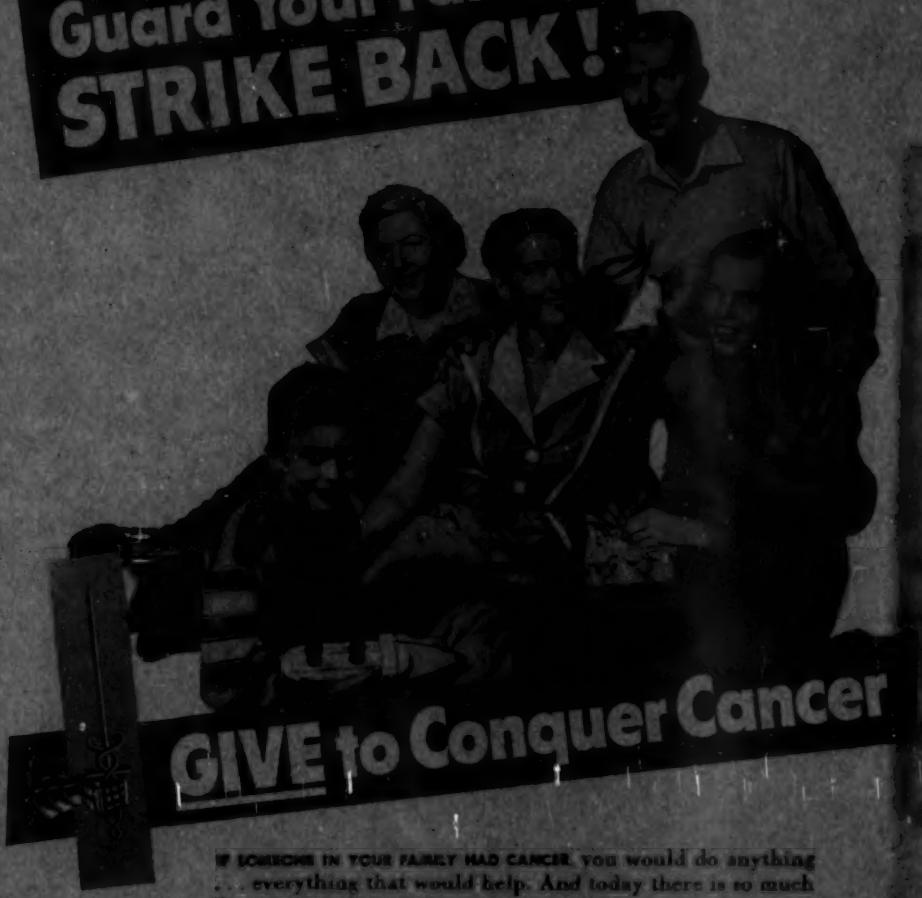

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100 mg. capsules, bottles of 25 and 100;
50 mg. capsules, bottles of 25 and 100.

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